On page 62, line 19, delete the word "year" and insert in its place --yeast--.

On page 72, line 7, delete the word "engineering" and insert in its place --engineered--.

IN THE CLAIMS:

Please amend the claims as follows:

Cancel claims 51-57, 65-71, and 79-88, without prejudice.

1. (Amended) A method of determining a consensus profile for [a particular biological response] perturbations to a cell type or organism, said method comprising identifying common response motifs among sets of [co-varying] cellular constituents in a plurality of response profiles, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different perturbation to said type of cell or organism, wherein said sets of cellular constituents co-vary under a plurality of perturbations or are co-regulated, and wherein said common response motifs constitute the consensus profile for said perturbations [are associated with the particular biological response].

5. (Amended) The method of claim 4, wherein the plurality of response [profile] profiles comprises more than 100 response profiles.

6. (Amended) The method of claim 1, wherein the perturbations are [particular biological response is a biological response] associated with a particular biological effect.

10. (Amended) The method of claim 1, wherein the sets of [co-varying] cellular constituents [comprise] consist of cellular constituents which are co-regulated.

11. (Amended) The method of claim 1, wherein the sets of [co-varying] cellular constituents [comprise] consist of cellular constituents which co-vary in the plurality of response profiles.

18. (Amended) The method of claim 17, wherein the objective statistical test comprises:

(a) determining an actual fractional improvement in cluster analysis of the cellular constituents;

(b) generating permuted response of cellular constituents by means of Monte Carlo randomization of [each response profile] perturbation index for the response of each cellular constituent across all perturbations;

(c) performing cluster analysis on the permuted response of cellular constituents;

(d) determining the fractional improvement in the cluster analysis on the permuted response of cellular constituents; and

(e) repeating said steps of generating permuted response of cellular constituents and performing cluster analysis on the permuted response of cellular constituents so that a distribution of fractional improvements is obtained[.];

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

23. (Amended) The method of claim 20, wherein said cluster analysis determines a clustering tree, [the cellular constituents which co-vary] the response profiles associated with similar biological effects comprising branches of said clustering tree.

24. (Amended) The method of claim 23, wherein the branches are selected by applying a cutting level across said clustering tree, said cutting level being determined by an expected number of biological pathways represented by the sets of cellular constituents [which co-vary].

25. (Amended) The method of claim 20, wherein a statistical significance for the sets of [co-varying cellular constituents] response profiles is determined by means of an objective statistical test.

26. (Amended) The method of claim 25, wherein the objective statistical test comprises:

(a) determining an actual fractional improvement in the cluster analysis of the response profiles;

(b) generating permuted response profiles by means of Monte Carlo randomization of cellular constituent index for each response profile across the measured cellular constituents;

(c) performing cluster analysis on the permuted response profiles;

(d) determining the fractional improvement in the cluster analysis on the permuted response profiles; and

(e) repeating said steps of generating permuted response profiles and performing cluster analysis on the permuted response profiles so that a distribution of fractional improvements is obtained[.];

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

27. (Amended) The method of claim 1, wherein the sets of [co-varying] cellular constituents [comprise] are basis cellular constituent sets.

29. (Amended) [The method of claim 27, further comprising prior to said identifying the step of converting the response profiles into projected response profiles by a method comprising projecting the response profiles onto the basis cellular constituent sets, wherein said projected response profiles are the response profiles of said identified common response motifs] A method of determining a consensus profile for perturbations to a cell type or organism, said method comprising identifying common response motifs among a plurality of projected profiles, each projected profile in said plurality of projected profiles

(i) resulting from a different perturbation to said type of cell or organism, and

(ii) comprising measurements of a plurality of cellular constituents in said type of cell or organism that have been projected onto basis cellular constituent sets, said basis cellular constituent sets being defined by co-variation of measurements of cellular constituents under a plurality of different perturbations, wherein said common response motifs constitute the consensus profile for said perturbations.

30. (Amended) The method of claim 1 wherein the consensus profile is the intersection of the sets of [co-varying] cellular constituents activated or de-activated in the common response motifs.

31. (Amended) The method of [claims 30] claim 29, wherein the [sets of co-varying cellular constituents comprise basis cellular constituent sets, and further comprising prior to said identifying the step of converting the response profiles into projected response profiles by means of projecting the response profiles onto the basis cellular constituent sets, wherein said projected response profiles are the response profiles of said identified] consensus profile is the intersection of the sets of cellular constituents activated or de-activated on the common response motifs.

38. (Amended) A method of determining a consensus profile for [a particular biological response] perturbations to a cell type or organism, said method comprising identifying common response motifs among sets of [co-varying genesets] genes in a plurality of response profiles, each response profile in said plurality of response profiles (i) comprising [expression profiles of] measurements of transcript levels for a plurality of genes, and (ii) resulting from a different perturbation to said type of cell or organism, wherein said sets of genes co-vary under a plurality of perturbations or are co-regulated, and wherein said common response motifs constitute the consensus profile for said perturbations [are associated with the particular biological response].

39. (Amended) A method for comparing a biological response profile to a consensus profile [provided by identifying], said consensus profile comprising common response motifs among [sets of co-varying cellular constituents in] a plurality of projected response [profile] profiles, each projected response profile in said plurality of projected response profiles

(i) resulting from a different perturbation to said type of cell or organism, and

(ii) comprising measurements of a plurality of cellular constituents in said type of cell or organism that have been projected onto basis cellular constituent sets, said basis cellular constituent sets being defined by co-variation of measurements of cellular constituents under a plurality of different perturbations, wherein said common response motifs constitute the

consensus profile for said perturbations [which are associated with a particular biological response], said method comprising:

(a) converting the biological response profile into a projected response profile by projecting measurements of cellular constituents in said biological response profile onto said [according to a definition of] basis cellular constituent sets[, wherein each of said basis cellular constituent sets comprises cellular constituents which co-vary in the plurality of response profiles]; and

(b) determining the value of a similarity metric between the projected response profile and the consensus profile.

44. (Amended) A method for grouping measured response profiles in sets which are associated with similar biological effects comprising [identifying] grouping sets of response profiles [based upon] among a plurality of response profiles, said sets of response profiles consisting of response profiles having similar responses of a [plurality] group of cellular constituents, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different perturbation.

50. (Amended) The method of claim 49, wherein the objective statistical test comprises:

(a) determining an actual fractional improvement in the cluster analysis of the response profiles;

(b) generating permuted response profiles by means of Monte Carlo randomization of cellular [constituents] constituent index for each response profile across the measured cellular constituents;

(c) performing cluster analysis on the permuted response profiles;

(d) determining the fractional improvement in the cluster analysis of the permuted response profiles; and

(e) repeating said steps of generating permuted response profiles and performing cluster analysis on the permuted response profiles so that a distribution of fractional improvements is obtained[.];

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

58. (Amended) A method for determining the therapeutic efficacy of a drug or drug candidate comprising identifying [sets] one or more groups of [response profiles having similar responses of a plurality of] sets of cellular constituents [to] in one or more [measured] response profiles associated with exposure to the drug or drug candidate , each response profile comprising measurements of a plurality of cellular constituents, wherein each of said groups [sets corresponds to] is indicative of a particular therapeutic effect, and wherein the therapeutic [efficacy] effect of the drug or drug candidate is determined to be the particular therapeutic effect indicated by [according to] the identified [sets] groups, wherein said sets of cellular constituents co-vary under a plurality of perturbations or are co-regulated.

59. (Amended) The method of claim 58, wherein the sets of [response profiles] cellular constituents are [identified] determined by a method comprising performing cluster analysis of the response profiles.

62. (Amended) The method of claim 59, wherein said cluster analysis determines a clustering tree, the sets of [response profiles] cellular constituents comprising branches of said clustering tree.

63. (Amended) The method of claim 59, wherein a statistical significance for the sets of [response profiles] cellular constituents is determined by means of an objective statistical test.

64. (Amended) The method of claim 63, wherein the objective statistical test comprises:

(a) determining an actual fractional improvement in the cluster analysis of [the response profiles] cellular constituents;

(b) generating permuted response [profiles] of cellular constituents by means of Monte Carlo randomization of the perturbation index for each cellular [constituents for each response profile] constituent across all perturbations;

(c) performing cluster analysis on the permuted response [profiles] of cellular constituents;

(d) determining the fractional improvement in the cluster analysis of the permuted response [profiles] of cellular constituents; and

(e) repeating said steps of generating permuted response [profiles] of cellular constituents and performing cluster analysis on the permuted response [profiles] of cellular constituents so that a distribution of fractional improvements is obtained[.];

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

72. (Amended) A method for analyzing response data from a biological sample comprising

(a) grouping cellular constituents from the biological sample into sets of cellular constituents that co-vary in a plurality of response profiles, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different perturbation to said [obtained from the] biological sample; and

(b) grouping the [biological] plurality of response profiles [obtained from the biological sample] into sets of [biological] response profiles that [effect similar] similarly affect cellular constituents.

73. (Amended) The method of claim 72, wherein one or more cellular constituents which co-vary in association with a particular biological effect are identified from the sets of cellular constituents that co-vary in [biological] said plurality of response profiles.

74. (Amended) The method of claim 72, wherein one or more response profiles that are associated with a particular biological effect are identified from the sets of [biological] response profiles that [affect similar] similarly affect cellular constituents.

75. (Amended) The method of claim 73 or 74, wherein the particular biological effect is an effect on a biological pathway.

76. (Amended) The method of claim 73, wherein the cellular constituents from the biological sample comprise a plurality of genes or gene transcripts, and one or more genes associated with [a particular] said biological effect are identified.

Add new claims as follows:

89. (New) The method of claim 1, wherein said sets of cellular constituents are co-varying cellular constituent sets.

90. (New) The method of claim 89, wherein the cellular constituents which co-vary are identified by cluster analysis.

91. (New) The method of claim 89, wherein the cluster analysis is done by means of a clustering algorithm.

92. (New) The method of claim 91, wherein the clustering algorithm is *hclust*.

93. (New) The method of claim 90, wherein said cluster analysis determines a clustering tree, the cellular constituents which co-vary comprising branches of said clustering tree.

94. (New) The method of claim 93, wherein the sets of co-varying cellular constituents are selected from a branching level of the clustering tree.

95. (New) The method of claim 90, wherein a statistical significance for the sets of co-varying cellular constituents is determined by means of an objective statistical test.

96. (New) The method of claim 95, wherein the objective statistical test comprises:

(a) determining an actual fractional improvement in cluster analysis of the cellular constituents;

(b) generating permuted response of cellular constituents by means of Monte Carlo randomization of the perturbation index for response of each cellular constituent across the set of perturbations;

(c) performing cluster analysis on the permuted response of cellular constituents;

(d) determining the fractional improvement in the cluster analysis on the permuted response of cellular constituents; and

(e) repeating said steps of generating permuted response of cellular constituents and performing cluster analysis on the permuted response of cellular constituents so that a distribution of fractional improvements is obtained,

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

97. (New) The method of claim 39, 40, 41, 42, or 43, wherein said sets of co-varying cellular constituents comprise cellular constituents which co-vary in the plurality of response profiles.

98. (New) The method of claim 72, wherein step (a) is carried out before step (b).

99. (New) The method of claim 72, wherein step (b) is carried out before step (a).

100. (New) A method of grouping sets of perturbations that similarly affect cellular constituents, among a plurality of perturbations comprising grouping a plurality of response profiles, said sets of response profiles consisting of response profiles having similar responses of a group of cellular constituents to said sets of perturbations, each response profile in said